

INTERNATIONAL PRELIMINARY EXAMINATION REPORT


(PCT Article 36 and Rule 70)

REC'D 10 JUN 2004

WIPO PCT

Applicant's or agent's file reference AXP/PG4789	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/03350	International filing date (day/month/year) 27.03.2003	Priority date (day/month/year) 28.03.2002
International Patent Classification (IPC) or both national classification and IPC C07D413/12, C07D413/12		
Applicant GLAXO GROUP LIMITED et al.		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of 5 sheets, including this cover sheet.
	<input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
	These annexes consist of a total of sheets.
3.	This report contains indications relating to the following items:
I	<input checked="" type="checkbox"/> Basis of the opinion
II	<input type="checkbox"/> Priority
III	<input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	<input type="checkbox"/> Lack of unity of invention
V	<input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	<input type="checkbox"/> Certain documents cited
VII	<input type="checkbox"/> Certain defects in the international application
VIII	<input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 30.09.2003	Date of completion of this report 09.06.2004
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Schuemacher, A Telephone No. +49 89 2399-7818



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/03350**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-40 as originally filed

Claims, Numbers

1-23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 22
because:
 - ☒ the said international application, or the said claims Nos. 22 relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the Standard.
 - ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-23
Inventive step (IS)	Yes: Claims	
	No: Claims	1-23
Industrial applicability (IA)	Yes: Claims	1-21,23
	No: Claims	

2. Citations and explanations

see separate sheet

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EXAMINATION REPORT - SEPARATE SHEET**

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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability:

Claim 22 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Novelty, Article 33(2) PCT:

Reference is made to the following documents:

- D1: DE 196 24 668 A (KLINGE CO CHEM PHARM FAB) (1998-02-19)
- D2: KATO S ET AL., JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 5, May 1990, pages 1406-1413, XP001037844
- D3: EP-A-0 903 349 (HOFFMANN LA ROCHE) (1999-03-24)

With regard to the prior art disclosed in the documents cited above the subject-matter of the present application, i.e N-(morpholin-2-yl)methyl acetamide derivatives does not appear to fulfil the requirements of novelty, cf. Article 33(2) PCT:

The prior art document D1 discloses a specific example of compound falling within the scope of present claim 1 (see Example n° 374 in Table I). Moreover, D1 anticipates the process of present claim 14 (see Verfahren A, p.65).

Document D2 discloses the compound n° 9 in scheme II, which is indeed the intermediate claimed in present claims 16 and 17.

Thus, the subject-matter of the present application cannot be considered to be new and the requirements of Article 33(2) PCT are not met.

2. Inventive step, Article 33(3) PCT:

The examining division wishes to formulate the following comment, which concerns **only** the compounds that have not been anticipated by the prior art documents:

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The Applicant appears to have set himself the task of making available further CCR-3 receptor antagonists, which blocks the migration/chemotaxis of eosinophils and thus possess anti-inflammatory properties, see p.3, I.21-23.

The compounds of D1 and D2 are used as immunosuppressants and as stimulants for upper gastrointestinal mobility/ antiemetic agents respectively.

Document D3, considered as the closest prior art document, discloses CCR-3 antagonists useful as anti-inflammatory agents (see p.45 I.42-47) but which structure contains a piperidine or a piperazine ring N-substituted with a benzyl group.

The man skilled in the art could not, when starting from the teaching of D3, arrive to the present claimed compounds in an obvious manner. The present application contains pharmacological data (p.18, I.4-10), which prove that some of the claimed compounds indeed possess the alleged activity. Thus, only for these tested compounds, which also satisfy the requirements for novelty, an inventive step based on their surprising CCR-3 antagonist activity could be acknowledged.

3. industrial applicability:

For the assessment of the present claim 22 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.